

IN THE CLAIMS:

Summary of Current Claim Amendments:

Please cancel Claims 4, 7, and 9 as follows, without prejudice to or disclaimer of the subject matter therein.

Please amend Claims 1, 2, 3, 6, 8, 10-18, and 38 as follows, without prejudice to or disclaimer of the subject matter therein.

Please add new Claims 43-49 as shown below.

Listing of Claims:

1. (Currently Amended) A chimeric fibroblast growth factor-2 (FGF-2), comprising:

a) a biologically active fibroblast growth factor-2 (FGF-2) protein having a first amino acid sequence that is encoded by a nucleic acid sequence that is at least about 70% identical to a nucleic acid sequence encoding a fibroblast growth factor-2 (FGF-2) protein represented by SEQ ID NO:5 or SEQ ID NO:6, wherein the FGF-2 protein has an FGF-2 biological activity selected from the group consisting of: promotion of cell proliferation, repression of terminal differentiation in a cell, promotion of angiogenesis, promotion of wound healing, promotion of osteogenesis, and promotion of nerve outgrowth; and,

b) a penetratin peptide having a second amino acid sequence, wherein the penetratin peptide is selected from the group consisting of:

i) a first peptide comprising an amino acid sequence selected from the group consisting of:

1) X₁-X₂-X₃-X₄-X₅-X₆-X₇-X₈-X₉-X₁₀-X₁₁-X₁₂-X₁₃-X₁₄-X₁₅-X₁₆; and,

2) X₁₆-X₁₅-X₁₄-X₁₃-X₁₂-X₁₁-X₁₀-X₉-X₈-X₇-X₆-X₅-X₄-X₃-X₂-X₁;

wherein X₁, X₂, X₃, X₄, X₅, X₇, X₈, X₉, X₁₀, X₁₁, X₁₂, X₁₃, X₁₄, X₁₅, and X₁₆ each represent an α -amino acid, between 6 and 10 of

which are hydrophobic amino acids; and wherein X₆ represents Trp;
and,

ii) a second peptide comprising amino acid residues 49-57 of
HIV Tat protein (SEQ ID NO:17),

wherein the biological activity of said penetratin peptide is to transports
transport said chimeric fibroblast growth factor-2 (FGF-2) across a lipid bilayer of
a cell independently of the presence of an FGF-2 receptor;

wherein said second amino acid sequence is linked to said first amino acid sequence;

and

wherein said chimeric fibroblast growth factor-2 (FGF-2) is characterized by:

i) said FGF-2 biological activity of (a) in the absence of heparan
sulfate, said chimeric FGF has fibroblast growth factor (FGF) biological
activity; and,

ii) entry into a living cell in the absence of a receptor that binds
to FGF-2.

2. (Currently Amended) The chimeric fibroblast growth factor-2 (FGF-2) of
Claim 1, wherein said chimeric FGF-2 has FGF biological activity that is characterized by:

a) repression of terminal differentiation in the absence of heparan
sulfate; and,

b) promotion of cell proliferation in the absence of heparan sulfate.

3. (Currently Amended) The chimeric fibroblast growth factor-2 (FGF-2) of
Claim 1, wherein said second amino acid sequence is linked to the N-terminus of said first
amino acid sequence.

4-5. (Cancelled)

6. (Currently Amended) The chimeric fibroblast growth factor-2 (FGF-2) of
Claim 1, wherein said ~~FGF protein comprises an~~ first amino acid sequence is selected from
the group consisting of SEQ ID NO:5 and SEQ ID NO:6.

7. (Cancelled)

8. (Currently Amended) The chimeric fibroblast growth factor₂ (FGF₂) of Claim 1, wherein said FGF₂ protein has an amino acid sequence comprising from position 18 through position 172 of SEQ ID NO:2 or from position 17 through 171 of SEQ ID NO:4.

9. (Cancelled)

10. (Currently Amended) The chimeric fibroblast growth factor₂ (FGF₂) protein of Claim 9₁, wherein said second peptide does not comprise amino acid residues 22-36 or 73-86 of HIV Tat protein (SEQ ID NO:17).

11. (Currently Amended) The chimeric fibroblast growth factor₂ (FGF₂) of Claim 9₁, wherein said first peptide is selected from the group consisting of a peptide comprising helix 3 of a homeobox domain and a homeobox domain.

12. (Currently Amended) The chimeric fibroblast growth factor₂ (FGF₂) of Claim 9₁, wherein said first peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:9, amino acid residues 42 through 58 of SEQ ID NO:9, amino acid residues 43 through 59 of SEQ ID NO:9, amino acid residues 43 through 58 of SEQ ID NO:9, amino acid residues 58 through 43 of SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, and SEQ ID NO:16.

13. (Currently Amended) The chimeric fibroblast growth factor₂ (FGF₂) of Claim 9₁, wherein said first peptide comprises amino acid residues 2-17 of SEQ ID NO:2.

14. (Currently Amended) The chimeric fibroblast growth factor₂ (FGF₂) of Claim 9₁, wherein said second peptide comprises an amino acid sequence from an HIV Tat protein selected from the group consisting of amino acid residues 37-72 of SEQ ID NO:17, amino acid residues 38-72 of SEQ ID NO:17, amino acid residues 47-72 of SEQ ID NO:17, amino acid residues 37-58 of SEQ ID NO:17, amino acid residues 38-58 of SEQ ID NO:17, amino acid residues 47-58 of SEQ ID NO:17, amino acid residues 1-21 and 38-72 of SEQ ID NO:17, amino acid residues 47-62 of SEQ ID NO:17, amino acid residues 38-62 of SEQ ID NO:17, amino acid residues 1-72 of SEQ ID NO:17, amino acid residues 1-58 of SEQ ID NO:17, and amino acid residues 48-60 of SEQ ID NO:17.

15. (Currently Amended) The chimeric fibroblast growth factor-2 (FGF-2) of Claim 91, wherein said second peptide comprises amino acid residues 48-60 of SEQ ID NO:17 or amino acid residues 2-14 of SEQ ID NO:4.

16. (Currently Amended) The chimeric fibroblast growth factor-2 (FGF-2) of Claim 1, wherein said chimeric fibroblast growth factor-2 (FGF-2) comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2 (HLX-FGF) and SEQ ID NO:4 (TAT-FGF).

17. (Currently Amended) The chimeric fibroblast growth factor-2 (FGF-2) of Claim 1, wherein said chimeric fibroblast growth factor-2 (FGF-2) is encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:1 (HLX-FGF) and SEQ ID NO:3 (TAT-FGF).

18. (Currently Amended) A therapeutic composition comprising the chimeric fibroblast growth factor-2 (FGF-2) of Claim 1 and a pharmaceutically acceptable excipient.

19-37. (Cancelled)

38. (Currently Amended) A method to repress terminal differentiation and promote proliferation in a cell, comprising administering to a cell a chimeric fibroblast growth factor-2 (FGF-2) ~~protein~~ according to Claim 1.

39. (Previously Amended) The method of Claim 38, wherein said cell has reduced heparan sulfate proteoglycan production characterized by a reduction in both repression of terminal differentiation and promotion of proliferation in the presence of naturally occurring fibroblast growth factor.

40. (Previously Amended) The method of Claim 38, wherein said cell is a cell of patient that has a condition selected from the group consisting of stroke, nerve damage, bone damage, muscle damage, and a wound.

41. (Previously Amended) The method of Claim 38, wherein said chimeric fibroblast growth factor (FGF) is administered to said cell *in vivo*.

42. (Cancelled)

43. (New) The chimeric fibroblast growth factor (FGF) of Claim 1, wherein said first amino acid sequence is encoded by a nucleic acid sequence that is at least about 80%

identical to a nucleic acid sequence encoding a fibroblast growth factor-2 (FGF-2) protein represented by SEQ ID NO:5 or SEQ ID NO:6, wherein the FGF-2 protein has an FGF-2 biological activity selected from the group consisting of: promotion of cell proliferation, repression of terminal differentiation in a cell, promotion of angiogenesis, promotion of wound healing, promotion of osteogenesis, and promotion of nerve outgrowth.

44. (New) The chimeric fibroblast growth factor (FGF) of Claim 1, wherein said first amino acid sequence is encoded by a nucleic acid sequence that is at least about 90% identical to a nucleic acid sequence encoding a fibroblast growth factor-2 (FGF-2) protein represented by SEQ ID NO:5 or SEQ ID NO:6, wherein the FGF-2 protein has an FGF-2 biological activity selected from the group consisting of: promotion of cell proliferation, repression of terminal differentiation in a cell, promotion of angiogenesis, promotion of wound healing, promotion of osteogenesis, and promotion of nerve outgrowth.

45. (New) The chimeric fibroblast growth factor (FGF) of Claim 1, wherein said first amino acid sequence is encoded by a nucleic acid sequence that is at least about 70% identical to 59 to 523 of SEQ ID NO:1 or to positions 59-523 of SEQ ID NO:3, wherein the FGF-2 protein has an FGF-2 biological activity selected from the group consisting of: promotion of cell proliferation, repression of terminal differentiation in a cell, promotion of angiogenesis, promotion of wound healing, promotion of osteogenesis, and promotion of nerve outgrowth.

46. (New) The chimeric fibroblast growth factor (FGF) of Claim 1, wherein said first amino acid sequence is encoded by a nucleic acid sequence that is at least about 80% identical to 59 to 523 of SEQ ID NO:1 or to positions 59-523 of SEQ ID NO:3, wherein the FGF-2 protein has an FGF-2 biological activity selected from the group consisting of: promotion of cell proliferation, repression of terminal differentiation in a cell, promotion of angiogenesis, promotion of wound healing, promotion of osteogenesis, and promotion of nerve outgrowth.

47. (New) The chimeric fibroblast growth factor (FGF) of Claim 1, wherein said first amino acid sequence is encoded by a nucleic acid sequence that is at least about 90% identical to 59 to 523 of SEQ ID NO:1 or to positions 59-523 of SEQ ID NO:3, wherein the

FGF-2 protein has an FGF-2 biological activity selected from the group consisting of: promotion of cell proliferation, repression of terminal differentiation in a cell, promotion of angiogenesis, promotion of wound healing, promotion of osteogenesis, and promotion of nerve outgrowth.

48. (New) The chimeric fibroblast growth factor-2 (FGF-2) of Claim 1, wherein said first amino acid sequence is SEQ ID NO:5.

49. (New) The chimeric fibroblast growth factor-2 (FGF-2) of Claim 1, wherein said first amino acid sequence is SEQ ID NO:6.